Author’s response to reviews

Title: Atypical acute retinal necrosis accompanied by Terson's syndrome : A case report

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Author’s response to reviews:

Reviewer reports:

Ester Carreño (Reviewer 1): Although an interesting case, there are important issues that need to be clarified before considering publication.

- There is a lack of spaces between words along the manuscript.

--> I would like to thank you for your valuable comments. I apologize for any confusion caused by these technical errors. I have reviewed the manuscript and revised the spacing between words.

- Intravitreal foscarnet is most commonly used than intravitreal ganciclovir worldwide, equally viral culture is currently abandoned as PCR technology is broadly used.

- Please rewrite introduction.

--> I agree that intravitreal foscarnet is used more commonly than intravitreal ganciclovir worldwide, and that PCR technology is currently preferred over viral culture. Accordingly, I have revised the Background section (page 4) as follows:

The diagnosis of ARN is usually based on clinical findings and the confirmation of the causative viral DNA using serum or intraocular fluid antibody testing, viral culture, retinal biopsy, and polymerase chain reaction (PCR) [7,8]. Nowadays, clinicians prefer testing focal samples rather than conducting a serum antibody titer for viruses. PCR analysis of the aqueous humor and
vitreous fluid samples is useful for identifying the origin of the virus and is currently the preferred method for viral diagnosis [9,10,11].

The initial treatment for ARN is intravenous acyclovir (1500 mg/m2/day) for 5–10 days, followed by oral acyclovir (800 mg five times/day) for 4–6 weeks. Intravitreal foscarnet or ganciclovir injections may also serve as adjunctive therapy for the management of ARN. Intravitreal foscarnet in combination with systemic antiviral therapy has been reported to improve visual and functional outcomes in patients with ARN [12,13].

I have also added the relevant references in the list on page 10.

References


- A positive serology does not confirm the diagnosis of ARN, the PCR positive for VZV confirms the diagnosis of VZV retinitis.

--> I agree with your opinion. Accordingly, I have made the necessary changes in the manuscript.

Polymerase chain reaction identified varicella-zoster virus DNA in the aqueous humor (page 3, lines 64 to 65).

Anterior chamber paracentesis and PCR analysis of the aqueous humor were performed. VZV DNA was identified in the aqueous humor, while DNA for HSV-1, HSV-2, and cytomegalovirus was not detected (page 6, lines, 119 to 1215).

- Not sure how Terson's syndrome was diagnosed. Did the patient had a subarachnoid haemorrhage? This is not clear as currently written. Fluorescein angiography at the moment of the vitreous haemorrhage could be helpful to prove that the vitreous haemorrhage was not secondary to retinal neovascularization due to the occlusive arteritis, which is rather more common than a Terson's syndrome.

-->Thank you for your comments. In the present case, there was no SAH, and FAG was not performed when the vitreous hemorrhage increased. However, a previous study has reported that Terson’s syndrome can develop because of a sudden increase in the intracranial pressure, in the absence of SAH. Fluorescein angiography revealed that the nonperfusion area was localized in the peripheral retina, and new vessels were not observed at the initial visit. Even though our
patient had been treated with intravenous acyclovir and oral prednisolone, his retinal lesions worsened. He developed a headache, so we performed spinal tapping in the Department of Neurology at our hospital; the intracranial pressure was found to be 31 mmHg. Brain MRI revealed a subacute or old hemorrhagic infarction in the right occipital lobe. Thus, we diagnosed Terson’s syndrome considering the sudden increase in the intracranial pressure. I have modified the Case Presentation section (page 65) and added the relevant reference in the list on page 10.

Spinal tapping was performed in the Department of Neurology at our hospital; the intracranial pressure was 31 mmHg. This indicated the possibility of Terson’s syndrome due to a sudden increase in the intracranial pressure [15].


- What was the time frame between intravitreal ganciclovir injections?

-->Five injections were administered from day 5 to day 15 of admission. I have mentioned this in the Case Presentation section (page 6, line 138).

- What was the dose of the oral prednisone/prednisolone?

-->I have added this information in the Case Presentation section (page 6, line 142).

-What was the evolution of the brain findings? Were this findings a consequence of viral encephalitis?

-->The lesions in the right occipital lobe could be indicative of viral encephalitis. However, in viral encephalitis, symmetrical lesions are seen in the left and right brain hemispheres, with thickening of the meninges. In the present case, however, the brain lesions were localized in the right hemisphere, and there was no evidence of meningeal thickening. In addition, a specialist in the Department of Radiology at our hospital interpreted the imaging findings as hemorrhagic infarction. Therefore, the lesions in our case were more likely to be associated with hemorrhagic infarction than with viral encephalitis.

Francesco Pichi (reviewer 2)

The Abstract is difficult to read because of extensive English misspells.

-->I apologize for the typographical errors. I have reviewed the manuscript and rectified these errors.

It is not very clear from reading the Abstract how the diagnosis of Terson was made; the MRI findings seems consistent with herpes encephalitis, or am I mistaken?
Subsequently, the patient complained of headache. Brain T2-weighted magnetic resonance imaging demonstrated a subacute or old hemorrhagic infarction in the right occipital lobe and contrast-enhancing lesions in the right basal ganglia. Spinal tapping was performed in the Department of Neurology at our hospital; the intracranial pressure was 31 mmHg.

The lesions in the right occipital lobe could be indicative of viral encephalitis. However, in viral encephalitis, symmetrical lesions are seen in the left and right brain hemispheres, with thickening of the meninges. In the present case, however, the brain lesions were localized in the right hemisphere, and there was no evidence of meningeal thickening. In addition, a specialist in the Department of Radiology at our hospital interpreted the imaging findings as hemorrhagic infarction. Therefore, the lesions in our case were more likely to be associated with hemorrhagic infarction than with viral encephalitis.

The conclusion of the Abstract is a bit far fetched... MRI can help identify "other causes of atypical clinical features of ARN accompanied with Terson's syndrome"? I am not sure about the meaning of this sentence.

I completely agree with your comments and have accordingly modified the Conclusions section in the Abstract (page 43).

The findings from this case suggest that intravitreal ganciclovir is an effective adjunctive therapy in the event of a poor response to conventional treatment in patients with VZV-associated ARN accompanied by Terson’s syndrome.

BACKGROUND

Some repetitions that render the reading difficult (retinal retinitis).

I apologize for the poor choice of words. I have now used the term “diffuse necrotizing retinitis” at the relevant instances in the Abstract (page 32) and Background (page 54).

Please remove the sentence "hemorrhage of the retina...is uncommon".

I have deleted the sentence as per your recommendation.

CASE PRESENTATION

Once again, no spaces between the words. The Authors seem not to have checked the pdf before approving the manuscript.
I apologize for any confusion caused by these technical errors. I have reviewed the manuscript and rectified the spacing between words and typographical errors.

Thank you for your comments. We performed spinal tapping for our patient when he complained of headache and found that his intracranial pressure was high at 31 mmHg. This sudden increase in the intracranial pressure suggested Terson’s syndrome. I have made the necessary changes in the Case Presentation section (page 65) and added the associated reference in the list on page 10.

Spinal tapping was performed in the Department of Neurology at our hospital; the intracranial pressure was 31 mmHg. This indicated the possibility of Terson’s syndrome due to a sudden increase in the intracranial pressure [15].

Reference


The images are striking but major editing to the manuscript language and clarification on the Terson diagnosis are necessary.

I sincerely appreciate your hard work and effort in reviewing our manuscript. The manuscript has now been reviewed by a native English speaker specialized in scientific editing. In addition, I have justified the diagnosis of Terson’s syndrome by adding the necessary information, as explained in previous responses.

Once again, I would like to thank the reviewers for their valuable comments, which we believe have considerably improved our manuscript. We hope the revised manuscript is now considered suitable for publication in BMC Ophthalmology.